NASA-CR-200955

FINAL
7N-52-CR

G7-7521

FINAL TECHNICAL REPORT NAG 2-536

TITLE: EFFECTS OF GRAVITY ON EYE MOVEMENTS AND NEURONAL ACTIVITY IN THE VESTIBULAR NUCLEI (OPTOKINETIC ACTIVATION OF VERTICAL VESTIBULAR NEURONS)

NASA GRANT NUMBER: NAG 2-536

The NASA Technical Officer for this grant is Nancy Daunton, Ph.D., NASA-Ames Research Center, Moffett Field, CA 94035

INSTITUTION: MOUNT SINAI SCHOOL OF MEDICINE
1 GUSTAVE L. LEVY PLACE
NEW YORK, NEW YORK 10029

PRINCIPAL INVESTIGATOR: Bernard Cohen, M.D.
Box 1135
Mount Sinai School of Medicine
1 Gustave L. Levy Place
New York, New York 10029

PERIOD COVERED BY THIS REPORT: January, 1984 - December, 1988

INVESTIGATORS:

TITLE	PERIOD OF WORK
Bernard Cohen, M.D., Principal Investigator,	1/1/84 - 12/31/88
Harvey Reisine, Ph.D., Co-Investigator	1/1/84 - 12/31/88
Theodore Raphan, Ph.D., Co-Investigator	1/1/84 - 12/31/88
Daniel Schiff, M.D., Co-Investigator	1/1/84 - 6/30/88

Bernard Cohen
12/21/89

DESCRIPTION: Two studies were done during the period of support covered in this report. One was related to alterations in single unit activity in the vestibular nuclei induced by changes in head position with regard to gravity (1). The second was a study of effects of gravity on roll eye movements (2). In addition, we wrote papers on habituation and adaptive modification of the vestibulo-ocular reflex (3) and on an anlysis of semicircular canal activity and its relation to semicircular canal planes (4). A summary of work done follows plus a bibliography listing presentations, abstracts and publications:

1. ACTIVATION OF VESTIBULAR NUCLEI NEURONS BY ROTATION ABOUT AXES TILTED FROM THE VERTICAL, (OFF-VERTICAL AXIS ROTATION, OVAR). (Pages 2,3)

2. ACTIVATION OF ROLL OKN AND OKAN BY ALTERATION OF STATIC HEAD POSITION WITH REGARD TO GRAVITY. (Pages 4,5)

3. HABITUATION AND ADAPTIVE MODIFICATION OF THE VESTIBULO-OCULAR REFLEX (VOR). (Page 6)

4. A GEOMETRIC ANALYSIS OF THE SEMICIRCULAR CANALS AND INDUCED ACTIVITY IN THEIR PERIPHERAL AFFERENTS. (Page 6)

SUMMARY OF WORK:

1. ACTIVATION OF VESTIBULAR NUCLEI NEURONS BY OVAR:

Background:

Subclasses of neurons in the vestibular nuclei receive input from the three semicircular canals on each side. Firing rates of these neurons primarily code head velocity in the plane of the activated canals. During constant velocity rotation about a vertical axis, canal-related neurons are activated, but their activity decreases over a time course that is longer than that of the canals (Goldberg and Fernandez 1971; Waespe and Henn 1977). Guedry (1965) and Benson (1966) were the first to show that rotation at a constant velocity about axes tilted from the vertical (off-vertical axis rotation, OVAR) causes continuous nystagmus. It has been clearly established that this nystagmus is caused by activation of the otolith organs, acting through a mechanism in the vestibular nuclei that we have labelled as 'velocity storage' (See Raphan and Cohen, 1985, for review). Relatively little is known about the activation of neurons in the vestibular nuclei during such rotation. The goal of this work was to determine how the firing frequencies of vestibular nuclei neurons, which are probably responsible for the nystagmus induced during OVAR, are altered by this stimulus.

Summary of Methods:

Single unit activity was recorded from the vestibular nuclei of two rhesus monkeys using tungsten microelectrodes. Neurons were classified by their response to sinusoidal rotation about axes normal to canal planes while animals were upright. A majority of the neurons demonstrated a change in activity during rotation in canal planes about a vertical axis, identifying them as canal-receiving neurons. Others were responsive to static head tilt, identifying them as otolith-receiving neurons. The animals were then subjected to visual stimulation, i.e., to full-field rotation.

Summary of Results:

Activity patterns of the canal-related units had characteristics of "vestibular-only" and "vestibular plus pause" units. Units which were related to lateral semicircular canal activation had firing rates proportional to the steady state level of horizontal slow phase eye velocity between $\pm$ 60 deg/sec. One subclass of units showed little oscillation about the steady state level. Another class of lateral canal related units showed a marked oscillation about the steady state level, phase-locked to head position. These units also responded during periods of horizontal optokinetic nystagmus (OKN), horizontal optokinetic after-nystagmus (OKAN) and per- and post-rotatory vestibular nystagmus with time constants consistent with those of a system processing the dominant time constant of the VOR, i.e., with velocity storage. Their responses during OVAR also appeared to be related to velocity storage.

Steady state discharge rates of vertical canal related neurons were weakly proportional to the steady state component of horizontal eye velocity during OVAR when the animals were rotated in the direction that evoked excitation, i.e., in the contralateral direction. During OVAR in the ipsilateral direction neuronal activity generally decreased to a constant value. Although these neurons generally did not show any change in discharge rate during static head tilts at various angles relative to the spatial vertical, they were strongly modulated during OVAR. The amplitude of the modulation increased with increases in head velocity and eye velocity. Otolith related units in the vestibular nuclei showed no evidence of velocity storage and were modulated in accordance with head position during OVAR.

Significance:

These data indicate that lateral and vertical canal related units in the vestibular nuclei encode eye velocity signals during OVAR. They receive input that arises in the otolith organs and output a motor signal to the oculomotor system to produce the eye velocities responsible for the continuous nystagmus that accompanies OVAR. The nature of the activation of the canal-related, vestibular nuclei neurons idicate that they have the activity that would be appropriate for coding the three-dimensional structure of velocity storage. The oscillations related to head position with regard to gravity in the lateral and vertical canal related units are of considerable interest, since the source of this activation is still not clear. Possibly this is accomplished through the velocity estimator in the vestibular system (Raphan and Cohen, 1988; Sturm and Raphan, 1988). The otolith related neurons are probably responsible for the modulation in eye position that occurs during each cycle of OVAR. A mathematical scheme was proposed for how the activity of the various neurons could be utilized to produce the bias component and modulation in slow phase velocity related to head position during OVAR. Two papers were presented at Neuroscience Society meetings (Reisine et al. 1986; Reisine et al. 1988), and a manuscript is in preparation.

References resulting from this research:

1. Reisine, H., Raphan, T., Cohen, B. Activity in the vestibular nuclei during off-vertical axis rotation (OVAR). Soc. Neurosci. Abstr. 12:773, 1986

2. Reisine, H., Raphan, T., Cohen, B., Katz, E. Signal processing in the vestibular nuclei during off-vertical axis rotation (OVAR). Soc. Neurosci. Abstr. 14:172, 1988.

3. Reisine, H., Raphan, T. Single unit activity in rhesus monkey vestibular nuclei during off-vertical axis rotation (In preparation).

2. DEPENDENCE OF ROLL EYE MOVEMENTS ON HEAD POSITION WITH REGARD TO GRAVITY:

Background:

Recent development of techniques for recording roll or torsional movements with eye coils has made it possible to characterize these movements. The goal of this research was to determine the nature of torsional eye movements in the monkey. In the course of this work we found a striking dependence of torsional optokinetic nystagmus (OKN) and optokinetic after-nystagmus (OKAN) on velocity storage and on head position with regard to gravity.

Summary of methods:

A method was developed to implant a scleral search coil on the top of the eye, and to record roll eye movements continuously, using the magnetic search coil technique of Robinson (1963). Three turns of teflon-covered, braided stainless steel wire were threaded under the superior rectus muscle and brought through Tenon's capsule. The coil was generally about 14 mms in diameter when it was in place. It was sutured to the sclera in three places at the front of the coil. The back of the coil sat under the superior rectus muscle which held it in place. A similar 14 mm coil was implanted around the limbus and sutured to the sclera in four places. The leads of the 'frontal plane' coil were also brought through Teneon's capsule to a plug implanted on the head. The 'roll' coil was activated by the lateral field coils to record the torsional component of eye movements. The same lateral field coils drove the frontal plane coil for recordings of the horizontal component of eye movement. The vertical component of eye movement was also recorded by the frontal plane coil, which was activated by field coils placed above and below the animal's head.

Animals were tested in a three-axis vestibular stimulator which has been described in detail elsewhere (Raphan et al. 1981; Cohen et al. 1987). The stimulator is surrounded by a optokinetic drum which can be rotated to provide visual field motion about any head axis in any position with regard to gravity. Recordings of eye movements and control signals were displayed on a paper writer and stored on FM magnetic tape for analysis.

Summary of Results:

Using this technique we investigated saccadic eye movements and optokinetic responses of animals while upright, and optokinetic and vestibular responses while supine and prone. There were occasional spontaneous torsional saccades with the head fixed, but they were much less frequent and smaller than saccades with horizontal or vertical components. Torsional quick phases or saccades were rarely larger than 10 degrees.

Roll vestibular nystagmus was induced with the animal supine and rotating about a vertical axis. The gain of the initial jump in slow phase eye velocity during constant velocity rotation was close to unity up to about 30 deg/s. Peak velocities were 110 deg/s for rotational velocities of 180 deg/s. The time constant of decay of roll vestibular nystagmus was longer than the peripheral time constant of the input in the vestibular nerve, indicating involvement of velocity storage.

Roll OKN, in response to rotation of the visual field about the animal's line of sight, was weak (less than 5 deg/s) with the animal upright, and there was little or no roll OKAN. In supine or prone positions, the same stimulus induced strong roll OKN, followed by typical OKAN. Maximum peak velocities of OKN were close to unity up to 20 deg/s and saturated at 35 deg/s. There was little initial jump or fall in slow phase velocity at the onset or end of OKN, and peak OKN values were close to those of OKAN. This suggests that roll OKN was primarily induced by activation of velocity storage.

There was a monotonic decline in peak slow phase velocity of OKN and OKAN and in the falling time constant of OKAN as the animals were statically tilted from supine or prone to upright or right or left ear down. Absolute velocities were higher in right or left ear down than in the upright position, suggesting an interaction of roll eye position with slow phase eye velocities induced by velocity storage. Falling time constants of roll OKAN were considerably longer than of horizontal OKAN in several animals, indicating that falling time constants in different planes can be separately habituated.

Significance:

The findings demonstrate that roll OKN and OKAN are maximal when the plane of the nystagmus is spatially horizontal, and minimal when the nystagmus plane is vertical. The data support the hypothesis that velocity storage is strongest when the axis of eye rotation, i.e., the velocity vector is aligned with the direction of the gravity (Raphan and Cohen 1988). Three abstracts were presented as a result of this study, one at a Neuroscience meeting, one at a Man In Space Symposium, and a third at the 1987 Barany Meeting. A paper describing these results is in preparation.

References resulting from this work:

1. Schiff, D., Cohen, B., Raphan T. Roll OKN and OKAN: Effects of head position on velocity storage in the monkey. Neurosi. Abstr. 12: 774, 1986.

2. Cohen, B., Schiff, D. Effects of gravity on roll OKN and OKAN in the monkey. 7th International Man in Space Symposium, Houston, Texas, Feb 10-13, 1986.

3. Cohen, B., Schiff, D. Roll eye movements; Comparative characteristics and implications for three-dimensional organization of the oculomotor system. Abstracts of the Barany Society Meeting, Bologna, Italy, June, 1987.

4. Cohen, B., Dai, M., Raphan, T. and Helwig, D. Influence of gravity on torsional eye movements and velocity storage in the monkey. In preparation.

ADDITIONAL PAPERS SUPPORTED BY THIS PROJECT:

Summary:

Additional references were supported by this projects. One is related to adaptation and habituation of the vestibular and oculomotor systems. We showed that habituation of the vestibulo-ocular reflex is strongly dependent on the nodulus and uvula, but that adaptive modification is unaffected by nodulo-uvulectomy. This work identifies the site of origin and the transmitter species (GABA) utilized in habituation of the dominant time constant of the VOR.

The second reference is related to spatial orientation of the semicircular canals system and of neurons related to the semicircular canals in the central vestibular system. This work demonstrates that there is a close correspondence between the planes of the semicircular canals as measured from anatomical specimens and as determined physiological methods using the best planes of response of semicircular canal afferents. It helps establish the spatial frame of reference that is used by the brain to code head movement.

1. Cohen, B., Cohen, H. Habituation and adaptive modification of the vestibulo-ocular reflex (VOR). In: Proceedings of the workshop on Nervous System Plasticity in Relation to Long-term Exposure to Microgravity Environment. M. Igarashi, K. Nute, S. MacDonald (eds). NASA, Space Biomedical Research Institute, USRA Division of Space Biomedicine, pp. 31-42, 1989.

2. Reisine, H., Simpson, J.I., and Henn, V. A geometric analysis of semicircular canals and induced activity in their peripheral afferents in the rhesus monkey. In: Representation of Three-Dimensional Space in the Vestibular, Oculomotor, and Visual Systems. B. Cohen, V. Henn (eds). Annals of the New York Academy of Sciences 545: 10-20, 1988.

Progress Report, Optokinetic Activation of Vertical Vestibular Neurons
NASA-Ames Grant NAG 2-336

Period covered by report: Dec. 1985 - Dec. 1986

Publications:

1. Resine, H., Raphan, T. and Cohen B. Activity in the vestibular nuclei during off-vertical axis rotation (OVAR). Soc. Neurosc. Abstr. 12: 773, 1986.

2. Schiff, D., Cohen, B. and Raphan, T. Roll OKN and OKAN: Effects of head position on velocity storage in the monkey. Soc. Neurosc. Abstr. 12: 774, 1986.

3. Schiff, D. and Cohen, B. Effects of gravity on roll OKN and OKAN in the monkey. Presented at 7th International Man in Space Symposium, Physiologic Adaptation of Man in Space, Houston, Texas, Feb. 10-13, 1986.

Personnel:
Harvey Reisine, Ph.D., Assistant Professor of Neurology, Co-Investigator
Bernard Cohen, M.D., Professor of Neurology, Principal Investigator
Theodore Raphan, Ph.D., Professor of Computer & Information Sciences, Brooklyn College
Daniel Schiff, M.D., Post-Doctoral Fellow

Description:
The aim of this research is to analyze the sensitivity of neurons in the vestibular nuclei that respond to movement of the surrounding visual field in the monkey's pitch or roll plane or in planes in between. We intend to determine how the sensitivity of these neurons is altered by changing the attitude of the head with regard to gravity. This goal has been approached in the following two ways:

1. Roll OKN and OKAN: In order to adequately measure the ocular responses of the monkeys tested in this series of experiments it became obvious that it was necessary to measure the component of eye movement in the roll plane. To date there has been no method for this. Therefore, we developed a technique for implanting a second coil on the top of the monkey's eye that measured the roll component of movement (The first coil, attached in the frontal plane of the eye, measures the vertical and horizontal components of movement). Immediately on development of this technique a striking finding came to light, namely that roll OKN and OKAN were strongly dependent on the position of the head with regard to gravity. When monkeys were upright their roll OKN was weak and there was little or no roll OKAN. When lying in the prone or supine positions, however, roll OKN was strong, rising to steady state velocities of 60 deg/sec or more. In addition, roll OKAN was strong and was followed by secondary OKAN. Analysis of the characteristics of the induced eye nystagmus indicate that the strong roll OKN and OKAN are produced by the velocity storage mechanism in the vestibular system and suggest that the otolith organs play a key role in suppressing storage for movements in the roll plane when upright. This has obvious

significance for Man In Space Programs since if the otolith organs were not to suppress information about head or surround movement in the roll plane in zero G, the low frequency characteristics of the VOR would be much different than on earth, possibly contributing to disorientation and space motion sickness.

2. Responses of vestibular neurons to off-vertical axis rotation (OVAR): The major aim of the research on this grant is to study the optokinetic responses of vertical vestibular neurons. However, we have run into a series of technical difficulties. These include:

(1) It was necessary to develop a new amplifier system for single unit recordings that would have low noise and a good common mode rejection ratio. This is now essentially complete and should facilitate future unit recordings. (2) It is necessary to rebuild our primate chair with support for the animals when they assume various positions with regard to gravity so that they will not move and cause us to lose unit isolation. A prototype chair has been designed and a new chair will soon be built. (3) It has become necessary to alter the control mode of the horizontal axis of our stimulator to allow it to hold the gimbal stationary while the primate axis and the optokinetic drum are oscillating. The horizontal axis is currently a velocity servo mechanism and small imbalances cause it to go into oscillation when all axis are on and operating. In January Neurokinetics, the manufacturer will come to New York and install a positional servo for the horizontal axis that should take care of this problem. The money for this will come from other projects but it will directly benefit this project since it will then be possible to command changes in gimbal position with the OKN drum giving continuous stimulation in the planes of the monkeys vertical semicircular canals.

In the meantime we have taken the opportunity to complete work on another gravity-related problem, namely the continuous nystagmus induced by off-vertical axis rotation (OVAR). Initial results were presented recently at the Neuroscience meeting. Neurons that receive activation from the lateral semicircular canals were shown to have continuous changes in firing rate during OVAR. The initial grouping of activated cells indicates that we should be able to account for both the velocity and positional signals reaching ocular motoneurons. The significance is that we should be able to specify more precisely how gravitational effects are mediated on the horizontal vertical and roll VOR during OVAR.

Plans for 1987:

1. Finish characterization of roll OKN and OKAN. This will entail experiments in which head position is changed and roll stimulation is given in different positions. We have also developed a flash photo technique for calibrating roll position. Papers will be written explaining the technique of coil implantation and the characteristics of roll movements.

2. Finish single unit studies of OVAR, analyze the data and write the results for publication.

3. Record activity of vertical vestibular neurons during surround movement in semicircular canal planes. Analyze the data and write the results for publicastion.

Proposed Budget for 1987:

Personnel:

Harvey Reisine, Ph.D.	21,951
Fringe Benefits (25%)	5,488
Total Direct Costs	27,439
Indirect Costs (64%)	17,561
Total Costs	45,000

Bernard Cohen

Jane Tsambis
Director Grants and Contracts
212-650-8761

Bernard Cohen, M.D.
Principal Investigator